REMARKS

This document is submitted in response to the Office Action dated October 26, 2006 ("Office Action").

Claims 2-11, 13-18 and 21-39 are currently pending, among which claims 7-9, 14, 17, 18, and 21-38 have been withdrawn. Applicants have amended claims 2-6, 10, 11, 13, 15, 16, and 39 to particularly and distinctively point out the subject matter that they deem as their invention. Support for the amendments can be found, e.g., at page 15, lines 9-12; and at page 22, line 18. No new matter has been introduced.

Claims 2-6, 10, 11, 13, 15, 16, and 39 will be under examination. Applicants respectfully request that the Examiner reconsider this application in view of the remarks below.

Rejection under 35 U.S.C. § 102

Claims 2-6, 10, 11, 13, 15, and 16 stand rejected as being anticipated by Yamaoka et al. ("Yamaoka"). See the Office Action, pages 3-4, section 5.

Independent claim 2, as amended, covers a conjugate containing an APC-targeting molecule (a mutated superantigen) coupled with an antigen. This conjugate binds to a Class II MHC molecule.

Yamaoka discloses GST-fusion superantigen mutants, in which the GST portion is fused to the N-terminal of the superantigen mutants. See page 5021, left column. This reference is silent as to whether these GST-fusion superantigen mutants are capable of binding to MHC Class II molecules.

As well known in the art, the N-terminal region of a superantigen is critical to its binding to a Class II MHC molecule. See Yamaoka, page 5021, right column. Accordingly, a skilled artisan would know that a peptide fused to the N-terminal of a superantigen would interfere with interaction between the superantigen and a Class II MHC molecule. Indeed, Applicants' own experimental data clearly demonstrated that pigeon cytochrome C peptide, when fused to the N-terminal of SPE-C, a superantigen, prevented SPE-C from binding to MHC Class II molecules. See Exhibit A. Thus, the GST-fusion superantigen mutants disclosed in Yamoaka would not bind to Class II MHC molecules as required by claim 2. Applicants thus submit that Yamoaka

does not anticipate claim 2 as it fails to disclose each and every limitation of this claim. Nor does it anticipate claims 3-6, 10, 11, 13, 15, and 16, all of which depend from claim 2, either directly or indirectly.

For the reasons set forth above, Applicants respectfully request that the Examiner withdraw this rejection.

Rejection under 35 U.S.C. § 112, Second Paragraph

Claims 2-6, 10, 11, 13, 15, 16, and 39 are rejected as being indefinite. More specifically, the Examiner alleges that the term "immunomodulator" recited in these claims is ambiguous as to the direction (positive or negative) and the degree of the immune responses that it modulates. See the Office Action, page 2, last paragraph. Applicants disagree.

Nonetheless, for the sole purpose of moving this application forward, Applicants have replaced the term "immunomodulator" with "conjugate" in these claims, thus mooting the Examiner's ground for rejection.

Rejection under 35 U.S.C. § 112, First Paragraph (Written Description)

The Examiner rejects claims 2-5, 11, 13, 15, 16, and 39 for lack of written description on three grounds, each of which is traversed below.

First, it is the Examiner's position that the specification does not support "said APC-targeting molecule includes **a Class II MHC binding site**" recited in claim 2. See the Office Action, page 5, seventh paragraph. Applicants disagree.

The Specification teaches that "said APC-targeting molecule is a molecule which is structurally a **superantigen** but for disrupted T cell receptor binding site such that the molecule has little or no ability to activate T cells." See page 3, lines 10-12. Based on this teaching, a skilled person in the art would readily know that the APC-targeting molecule is a **mutated superantigen**. The Specification also teaches that "[s]uperantigens are a family of semi-conserved bacterial proteins that target the immune system by binding simultaneously to the T cell Receptor (TcR) via the Vb domain on T lymphocytes and **MHC class II molecules** expressed on APC including dentritic cells." See page 2, lines 1-4. According to this teaching, a skilled artisan would understand that all superantigens contain a **Class II MHC binding site**. As

the "APC-targeting molecule" recited in claim 2 is a superantigen mutant, he or she would readily appreciate that it contains **a Class II MHC binding site**. Indeed, the Specification further discloses that "[a]ll [superantigen] mutants are also assessed for their ability to bind to MHC class II by a number of assays including direct binding to MHC class II expressing B cells as well as Biacore studies with soluble forms of both superantigen mutant and MHC class II." See page 15, lines 9-12. This statement clearly indicates that the superantigen mutants include **a Class II MHC binding site**.

In view of the above remarks, Applicants submit that the Specification fully supports the term "said APC-targeting molecule includes a Class II MHC binding site" recited in claim 2.

Second, the Examiner alleges that the Specification does not support the term "the T-cell binding site having one or more mutations that **reduce its T cell proliferation activity**" recited in claim 2. See the Office Action, page 5, seven paragraph. Applicants disagree.

The Specification discloses "disrupted T cell receptor binding site such that the molecule has little or no ability to activate T cells." See page 3, lines 10-12. It further teaches determining the loss of T cell activation activity by T cell proliferation assays. See page 15, lines 8-9. Based on these teachings, one skilled in the art would have no doubt that a disrupted T cell binding site that has little or no ability to activate T cells would certainly display reduced T cell proliferation activity, which reflects the loss of T cell activation activity. Applicants therefore submit that the Specification supports the term "the T-cell binding site having one or more mutations that **reduce its T cell proliferation activity**" recited in claim 2.

Third, the Examiner asserts that the Specification does not support the term "reduces the T cell proliferation activity to equal to or greater than 10,000 folds" recited in claim 39. More specifically, it is the Examiner's position that "the instant specification on page 21 discloses specific targeting molecules such as SMEZ-2 W75L that reduce T cell proliferation to greater than 10,000 folds. However, this specific example is not adequate to support the more generic claims of the instant application which are drawn to an immunomodulator comprising any superantigen with any mutation in the T cell binding site." See the Office Action, page 5, last paragraph. Applicants disagree.

Claim 39 covers a subset of APC-targeting molecules (superantigens) with mutations in their T cell binding sites, i.e., those having reduced T cell proliferation activity to equal to or

greater than 10,000 folds compared to superantigens containing wild type T-cell receptor binding sites.

The Specification teaches amino acid residues that are part of the T cell binding sites of various superantigens and methods of screening for mutants that have reduced T cell proliferation activity. See Table 2 at page 16; and Example 3 at pages 16-18. Further, it fully describes several mutants, such as SMEZ-2 W75L, SMEZ-2 D42N, SMEZ-2 W75L.D42N.K182Q, SPE-C Y15, or SPE-C R181, that satisfy the requirement of claim 39, i.e., having reduced T cell proliferation activity to equal to or greater than 10,000 fold. See Table 2 at page 16 and Table 3, at page 21. These mutants constitute a representative number of species within the subset superantigen mutants covered by claim 39. Thus, there can be no doubt that Applicants were in full possession of the genus of mutants encompassed by claim 39. In other words, the Specification fully supports the term "having reduced T cell proliferation activity to equal to or greater than 10,000 folds compared to superantigens containing the wild-type T-cell receptor binding sites."

For the foregoing reasons, Applicants respectfully request withdrawal of this rejection.

CONCLUSION

In view of the above remarks, Applicants submit that claims 2-6, 10, 11, 13, 15, 16, and 39, as amended, are in condition for allowance. Favorable consideration of these claims is respectfully solicited.

Enclosed is a $510 check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 4/24/07

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